Classification of congenital lung cysts and malformations

Minnesota Society of Pathologists Fall Meeting
October 29, 2016

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History of congenital lung cysts

- Documented as early as 1859
- Chin & Tang 1949 – Congenital adenomatoid malformation
- Van Dijk 1972 – Congenital cystic adenomatoid malformation (cystic, intermediate, solid)
- Stocker 1977 – CCAM types 1, 2, 3
- Stocker 1994 – CCAM types 0, 1, 2, 3, 4

Stocker Classification, current

- “Congenital Pulmonary Airway Malformation” (CPAM)
- Type 0 CPAM, acinar dysgenesis (1-2%)
- Type 1 CPAM, large cyst type (65%)
- Type 2 CPAM, medium cyst type (10-15%)
- Type 3 CPAM, solid/adenomatoid type (5-8%)
- Type 4 CPAM, peripheral cyst type (10-15%)

Conceptual relationship to anatomy


CPAM type 0

- Acinar dysplasia/dysgenesis
- Described in 1986.
- Severe, diffuse, bilateral. Unresectable and incompatible with life. Survive a few hours.
- Term or preterm, immediate respiratory distress.
- Reported in siblings, likely genetic.

CPAM type 1

- “Large cyst” type
- Usually first week to month, but also adolescents
- Single or multiple large cysts (3-10cm), surrounded by smaller cysts.
- Lined by ciliated columnar epithelium; muscle, cartilage
- 45% with mucigenic cells, precursor to BAC

CPAM type 2
- "Medium/small cyst" type
- "Exclusively in 1st year of life"; "poorer outcome due to associated anomalies"
- Smaller cysts (0.5-2 cm); "Back-to-back" bronchiolar structures; thin muscular layer
  - Rhabdomyomatous dysplasia
  - No cartilage or mucigenic cells
- Seen in 50% of ELS.

CPAM type 3
- "Small cyst", "solid", "adenomatoid"
- First days-months of life; high mortality; polyhydramnios, fetal hydrops
- Large unilateral mass; lobe or lung.
- Small cysts (<0.2 cm); resembles immature lung; stellate irregular bronchiolar structures.
- No mucigenic epithelium, cartilage, or skeletal muscle.

CPAM type 4
- "Peripheral cyst" type
  - "hamartomatous proliferation of the distal acinus"
- Newborn to 4 years.
  - Single lobe (80%); rarely bilateral
  - Respiratory distress +/- PTX
- Large air-filled cysts
  - Lined by alveolar epithelial cells or low columnar epithelium.
  - Loose mesenchymal tissue with prominent vasculature.

Problems with CPAM classification
- Stocker classification is not comprehensive.
  - Lesions not included: bronchial atresia, ELS, ILS, bronchogenic cyst
  - Some lesions do not fit "classic patterns", ex. fetal
- "CPAM" encompasses broad morphologic spectrum
- Based on gross and microscopic anatomy, not pathogenesis
- No standard criteria, definitions or terminology bridging disciplines
  - Pathology, radiology, pediatric and fetal surgery, maternal-fetal medicine, pediatric pulmonary medicine, neonatology
  - A very confusing medical literature:
    - CCAM vs. CPAM, CPAM with sequestration (hybrid lesion?)
    - Misidentification of cystic PPB as CPAM

Langston Classification
- **Stocker type 0** = Acinar dysgenesis
- **Stocker type 1** = CPAM, large cyst type
- **Stocker type 2** = Intrauterine bronchial obstruction (bronchial atresia) sequence
  - Microcystic developmental abnormality seen in BA, ILS (BA with systemic arterial / venous connection), and ELS
- **Stocker type 3** = Pulmonary hyperplasia (adenomatoid or solid type)
- **Stocker type 4** = Pleuropulmonary blastoma, type 1

Bronchial Atresia - the hidden pathology

- Bronchial atresia sequence
  - Pattern of maldevelopment widely associated with airway obstruction (bronchial atresia, ILS, ELS)
  - Rarely without identifiable airway obstruction
- Common finding in many types of developmental lung lesions
  - 22/25 lung resections of IUUS identified lesions at Children’s Hospital Boston assessed for bronchial atresia
    - 14 CPAM, 9/13 assessed with BA
    - 3 CLO, 2/3 with BA
    - 1 ELS with BA
    - 1 ILS (not assessed)
    - 6 CPAM/seq 5/5 assessed with BA


Bronchial Atresia

- Isolated
  - Segmental or subsegmental
  - Formerly rarely seen in infancy
    - Later presentations: incidental x-ray finding, recurrent pneumonia, or dyspnea
  - Now common pathology of many IUUS lesions
    - Usually asymptomatic at birth
  - Gross pathology
    - Lobar enlargement, sometimes pseudofissures
    - Bulge at hilum sometimes marks atretic bronchus
    - Sub hilar mucocele and mucus in regional airways
    - Microcystic parenchymal maldevelopment, hyperinflation

Segmental bronchial atresia
RLL segmental BA with microcystic maldevelopment
8 day old

Extralobar sequestration
Left sided ELS with microcystic maldevelopment and lymphangiectasis associated with RLL ILS; prenatal dx, resected at 3 months

Infradiaphragmatic mass seen by prenatal US, accessory lung with esophageal bronchus

9 month old male infant with lung lesion identified on prenatal ultrasound. No respiratory problems at birth; RLL removed electively at 9 months.
Lobe weight 74.2 gm.
Expected R lung wt 53 gm.
Bronchial atresia is a gross diagnosis made by carefully examining the lobe or lung specimen. Microscopic examination alone can only suggest the diagnosis.

- Section lungs and lobectomies in a parasagittal plane, moving lateral to medial.
  - Segmental distribution of cysts.
  - Mucus stasis with central mucocele.
  - Point of atresia identified by retrograde probe of most dilated bronchial profile/cyst.

Bronchial Atresia and Sequestration

- BA with Systemic Vascular Connection
  - Also called: Intralobar sequestration (ILS)
  - Except for systemic vascular connection, identical gross and histology with isolated
  - More frequent in left lower lobe
  - Systemic artery usually single and from distal thoracic or proximal abdominal aorta, but multiple vessels and a wide variety of origins reported
  - Systemic venous connection, less common

- Intralobar sequestration is congenital (not acquired).
  - Numerous examples detected prenatally.
  - Examples of ILS and ELS in same patient.
Extralobar Sequestration

- Aberrant pulmonary mesenchyme develops apart from the normal lung; "accessory lobe"
- Location
  - usually thoracic (L>R)
  - anterior or posterior mediastinum, infradiaphragmatic, retroperitoneal typically near adrenal
- Relation to adjacent tissues
  - Systemic artery typically from descending thoracic aorta
  - Rarely communicates with esophagus or stomach
- Associated abnormalities - congenital diaphragmatic hernia
- Often asymptomatic
  - Sometimes hydrothorax, fetal hydrops, death

4 day old infant girl with congenital diaphragmatic hernia repair.
Complex Bronchopulmonary Foregut Malformation

Bronchogenic Cyst

Congenital lobar overinflation
Bronchomalacia, webs, stenoses, airway compression by vascular structures

CPAM 3
Massively enlarged lung, preterm stillborn – multilobar bronchial narrowing
Pulmonary hyperplasia
(19-20 wga)
Due to laryngeal
atresia

4 month old male infant with prenatal
diagnosis of 5 cm cystic lesion in LUL.
Pleuropulmonary Blastoma

- **TYPE 1** Cystic (low-grade)
- **TYPE 2** Cystic and solid
- **TYPE 3** Solid (high-grade)

- Type 1 (purely cystic) PPB is easily mistaken for Stocker type 4 CPAM (peripheral large cyst type).
  - Is type 4 CPAM an underdiagnosed, undersampled, or regressed type 1 PPB? Yes!

PPB: Associated Neoplasms

- Germline DICER1 abnormalities in PPB families
- Dysplastic/neoplastic diseases in 25% of PPB patients' relatives, often siblings
- Multicentric PPB, PPB in siblings/cousins
- Cystic nephroma, Wilms tumor
- Ovarian/testicular Sertoli-Leydig cell tumors
- Germ cell tumors
- Lymphoma/leukemia
- Thyroid malignancy
- Pituitary blastoma
- Various sarcomas...
Pathogenesis of congenital lung cysts

- Acinar dysgenesis (CPAM 0): Diffuse developmental/genetic disorder
- CPAM 1: Unknown
  - benign cystic neoplasm vs. malformation
- BA/ILS/ELS (CPAM 2): Bronchial obstruction in utero
- CPAM 3: Unknown
  - hyperplasia vs. neoplasm vs. hamartoma
- PPB type 1 (CPAM 4): Neoplasm

Congenital lung malformations, surgical specimens, cumulative data from 11 year review (1990-2000, Houston) and 10 year review (2000-2009, Denver)

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Time for re-classification?

- Our goal should be to re-define and classify according to pathogenesis
  - CPAM 1 and CPAM 3 remain poorly understood
- Stocker classification describes a set of morphologic patterns, which should lead to search for underlying etiology
  - Clinical – imaging – gross – microscopic correlation
  - CPAM 2 pattern – bronchial atresia sequence
  - CPAM 4 pattern – regressed/undersampled cystic PPB

22 wga fetus with 4.8 cm RUL lung mass.
Fetal surgery at 22 2/7 wga.
Lobe wt 37.7 gm

25 3/7 wga fetus, 6-7 cm RLL cystic and solid mass by ultrasound.
Lobectomy by fetal surgery at 25 6/7 wga.
Lobe wt 21.4 gm
Conclusion: Future goals

- Resolve pathogenesis of large cyst CPAM (type 1)...
- Resolve pathogenesis of solid CPAM (type 3)...
- Provide definitions of cystic lung malformations which are inclusive of fetal phenotypes...
- Unify terminology used by pathologists and other medical disciplines...